STATUS OF CLAIMS

The Examiner has acknowledged Appellants' prior brief accurately stated the status of the claims.

STATUS OF AMENDMENTS

The Examiner has acknowledged Appellants' prior brief accurately stated the status of amendments.

SUMMARY OF INVENTION

The Examiner has stated that the summary of invention contained in Appellants' prior brief is deficient because the summary states that the polypeptide has utility, and whether the claimed invention has utility is the issue before the Board.

The claims of the present application are directed to Fibroblast Grown Factor-CX (*i.e.*, "FGF-CX") polypeptides having homology to members of the Fibroblast Growth Factor (FGF) family of proteins. The FGF-CX polypeptide that is specifically recited in the claims involved in this appeal is the polypeptide comprising the amino acid sequence of SEQ ID NO:2. The specification and working examples demonstrate that the claimed FGF-CX protein stimulates cell growth, including the growth of cells in the lining of the gastrointestinal tract, such as epithelial cells and fibroblasts.

ISSUES BEFORE THE BOARD

The Examiner has acknowledged Appellants' prior brief accurately stated the issues before the Board.

GROUPING OF CLAIMS

The Examiner has acknowledged Appellants' prior brief accurately stated the grouping of claims.

CLAIMS APPEALED

The Examiner has acknowledged Appellants' prior brief contained in the Appendix an accurate copy of the appealed claims. These are reproduced herein in the Appendix.

ARGUMENTS

The Utility Rejection

The Examiner contends that Appellants' arguments to establish utility are not persuasive. The Examiner contends that the claimed invention lacks a substantial utility for two main reasons.

First, the Examiner contends that the disclosure of the utility of stimulating growth of fibroblasts and epithelial cells in the lining of the gastrointestinal tract is not substantial since it is but one disclosed utility among a disclosure of multiple utilities. According to the Examiner, "a skilled artisan would need to carry out further research on the claimed invention to determine which of the possible asserted uses the claimed invention could be used for; this does not constitute a disclosure of substantial utility." Examiner's Answer page 12.

Second, the Examiner contends that the disclosed utility of stimulating growth of fibroblasts and epithelial cells in the lining of the gastrointestinal tract is not a substantial utility, because Appellants' supporting data is shown *in vitro*, and the Examiner contends that *in vivo* data is required and the Examiner contends that Appellants' assertions of a utility of fibroblast proliferation based on homology are insufficient (even though those assertions are correct).

Appellants disagree.

Appellants' Assertions Regarding Utility Are Presumed True

Both case law and the MPEP direct the Patent Office to presume that a statement of utility made by an applicant is true. *See* MPEP 2107.02; *In re Langer*, 503 F.2d at 1391, 183 USPQ at 297; *In re Malachowski*, 530 F.2d 1402, 1404, 189 USPQ 432, 435 (CCPA 1976); *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). Appellants have clearly asserted that the claimed composition has utility in stimulating growth of fibroblasts and epithelial cells in the lining of the gastrointestinal tract. The Examiner concedes this.

Appellants' assertion of utility carries a presumption of truth.

It is the Examiner's burden to overcome this presumption. See MPEP 2107.02; *Raytheon v. Roper*, 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983) cert. denied, 469 U.S. 835 (1984). To overcome the presumption of truth, the Patent Office must respond with factual evidence to prove the assertion is not true.1/ Here the only evidence of record demonstrates that Appellants' asserted utility of stimulating growth of fibroblasts and epithelial cells in the lining of the gastrointestinal tract is true.

In order to rebut the applicant's presumption of utility, the Patent Office must make a *prima facie* showing that the claimed invention lacks utility, and provide a sufficient evidentiary basis for factual assumptions relied upon in establishing the prima facie showing. *In re Gaubert*, 524 F.2d 1222, 1224, 187 USPQ 664, 666 (CCPA 1975) ("Accordingly, the PTO must do more than merely question operability - it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability."). If the Office cannot develop a proper prima facie case and provide evidentiary support for a rejection under 35 U.S.C. § 101, a rejection on this ground should not be imposed. See, e.g., *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) ("[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a prima facie case of unpatentability ... If examination at the initial stage does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent."). See also *Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 USPQ 848 (Fed. Cir. 1985) (applying prima facie case law to 35 U.S.C. § 101); *In re Piasecki,* 745 F.2d 1468, 223 USPQ 785 (Fed. Cir. 1984).

There is no evidence of record here proffered by the PTO to support a rejection under 35 U.S.C. § 101. To the contrary, the only evidence of record clearly demonstrates that the Appellants' asserted utility for the claimed composition is accurate:

1/ The evidentiary standard used in *ex parte* examination is a preponderance of the totality of the evidence. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) ("[P]atentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument."); *In re Corkill*, 771 F.2d 1496, 1500, 226 USPQ 1005, 1008 (Fed. Cir. 1985). A preponderance of the evidence exists when it suggests that it is more likely than not that the assertion in question is true. *Herman v. Huddleston*, 459 U.S. 375, 390 (1983).

1. The claimed protein does, in fact, stimulate proliferation of fibroblasts (see, e.g., examples 9, 10, and 11).
2. The utility of the claimed protein was confirmed in Appellants' subsequent work, which demonstrates that the claimed protein does, in fact, stimulate proliferation of fibroblasts and epithelial cells in the lining of the gastrointestinal tract both *in vitro* and *in vivo*. See Jeffers et al., Gastroenterology, 123, pp. 1151-1162 (2002) (copy previously made of record).
3. In addition, Appellants submitted a Press Release announcing the FDA approval of CuraGen's (the assignee of this application) Investigational New Drug application to initiate human clinical trials using FGF-CX to treat oral mucositis by stimulating fibroblast proliferation in gastrointestinal tissue. Oral mucositis is a side effect of chemotherapy and radiotherapy resulting in the degradation of mucosal gastrointestinal tissue that can range from redness and irritation to severe ulcerations of the mouth and throat (copy previously submitted).
4. Utility is also supported by the structural similarity of FGF-CX with other known members of the FGF family, including conserved family domain and hydrophobic transport domain (see page 91, lines 3 to 7 of the specification as filed), and by the fact that the claimed FGF-CX polypeptide has a fibroblast proliferation activity like structurally related fibroblast growth factor-9 (FGF-9) which was already known and tested in the art for proliferation of fibroblasts (see pages 76 and 77 of the specification as filed along with FIGS. 4 and 5). 2/

The Examiner has not made out a *prima facie* case – the Examiner has presented no factual evidence to overcome the presumption of truth, nor any evidence that counters the above evidence that would lead one skilled in the art to question the objective truth of Appellants' statement of operability. And on the preponderance of the totality of the evidence here (whether or not a *prima facie* has been made out by the PTO), the record is clear that Appellants' asserted utilities of fibroblast proliferation and stimulation of epithelial cells in

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2/ The Examiner argues that utility is negated because the claimed protein and FGF-9 do not have an identical suite of biological activities. The ordinarily skilled artisan would not expect each member of a family of protein to have an identical suite of biological activities, but here Appellants identified a key common activity – proliferation of fibroblasts. That is all that is required.

the gastrointestinal tract are, in fact, true. And here there is a further presumption in favor of the Appellant because the claimed protein has entered human clinical trials for an asserted utility – section 2107.03 (IV) of the MPEP expressly states that "as a general rule, if an applicant has initiated human clinical trials for a product or process, Office personnel should presume that the applicant has established that the subject matter of that trial is reasonably predictive of having the asserted therapeutic utility." (emphasis in original).

For this reason, the utility rejection should be withdrawn since the evidence of record makes clear that the utility requirement has been satisfied.

Multiple Statements of Utility Do Not Render Invention Lacking Utility

The Examiner acknowledges that the specification teaches that the claimed invention may be used to stimulate cells of the gastrointestinal tract. See Examiner's Answer, page 11. However, the Examiner concludes that this acknowledged utility is not sufficient to meet the statutory utility requirement because this disclosed utility is "but one in a list of unrelated uses".3/ See March 4, 2003 Advisory Action, paragraph 5. The standard is simply that one credible utility be disclosed (and that is the case here) -- whether more than one utility is disclosed is irrelevant.

The PTO instructs its Examiners that "It is common and sensible for an applicant to identify several specific utilities for an invention, particularly where the invention is a product (e.g., ...a composition of matter)." See MPEP 2107.02. The MPEP continues that regardless of how many utilities are asserted, an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. § 101 and 35 U.S.C. § 112.

The case law is also crystal clear. Multiple additional statements of utility, even if several are not credible, do not render the claimed invention lacking in utility. *See, e.g., Raytheon v. Roper*, 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983), cert. denied, 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."); *In re Gottlieb*, 328 F.2d 1016, 1019, 140 USPQ 665, 668 (CCPA 1964) ("Having found that the antibiotic is useful for some

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3/ Appellants note that virtually all of the uses for the claimed protein are not unrelated – rather they are virtually all related to the protein's fibroblast proliferation activity, which the Examiner does not dispute was asserted. See Examiner's Answer p. 11.

purpose, it becomes unnecessary to decide whether it is in fact useful for the other purposes 'indicated' in the specification as possibly useful."); *In re Malachowski*, 530 F.2d 1402, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988).

Here, Appellants have clearly made one credible assertion of utility -- that the claimed protein can stimulate proliferation of fibroblast cells and epithelial cells and can therefore be used to treat wounds where cell proliferation is important, for example by treating ulcers in the lining of the gastrointestinal tract. The Examiner has acknowledged this. This is all that is required -- utility for the claimed protein has been established. To conclude otherwise would lead to the incorrect result, notwithstanding the undisputed fact that Appellants correctly asserted a credible, substantial, real world utility, that the assertion of other utilities somehow negates this accurate assertion of utility.

Requirement of In Vivo Activity Is Not Required

The Examiner's Answer states that Appellants' arguments are not persuasive because the Examiner contends that the "Examples on which Appellants' conclusions [as to utility] are based are not predictive of the biological activity of the claimed invention *in vivo*." See Examiner's Answer p. 9. This is not the standard for utility.

First, as noted above, Appellants' assertion of utility carries a presumption of truth and the Examiner has not presented any evidence that would lead the ordinarily skilled artisan to question the objective truth of Appellants' assertion – and as discussed above, the only evidence of record supports Appellants' assertion of utility.

Second, it is well-established law that "utility in the form of pharmacological activity in an *in vitro* setting satisfies the practical utility requirement of the *Manson* doctrine since establishing the existence and order of potency of such activity is the first link in a screening chain to identify compounds with *in vivo* activity and possible human therapeutic application." *See Chisum* 4.02[2](d). *See also Cross v. Iizuka*, 753 F.2d 1040, 1051, 224 USPQ 739, 747-4 (Fed. Cir. 1985) ("We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the

benefit provided by the showing of an *in vivo* utility."); *Fujikawa v. Wattansin*, 93 F.3d 1559, 1563, 39 USPQ2d 1895, 1899 (Fed. Cir. 1996), ("In the pharmaceutical arts, our court has long held that practical utility may be shown by adequate evidence of any pharmacological activity.")

Based on this well established law, the PTO instructs its Examiners in MPEP 2107.03 that "if reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process."4/ The PTO also instructs its Examiners that the Federal courts are not particularly receptive to rejections under 35 U.S.C. § 101 based on inoperability, and in cases where an applicant supplied a reasonable evidentiary showing supporting an asserted therapeutic utility, almost uniformly the 35 U.S.C. § 101-based rejection was reversed.5/

Courts have repeatedly found that the mere *in vitro* identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement. As the Court of Customs and Patent Appeals held in *Nelson v. Bowler*:

> "Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility." *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980).

4/ The PTO, in MPEP 2107.01, also reminds the Examiners that usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development.

> Office personnel should not construe 35 U.S.C. § 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans. *See, e.g., In re Sichert*, 566 F.2d 1154, 196 USPQ 209 (CCPA 1977); *In re Hartop*, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); *In re Anthony*, 414 F.2d 1383, 162 USPQ 594 (CCPA 1969); *In re Watson*, 517 F.2d 465, 186 USPQ 11 (CCPA 1975).

5/ See, e.g., *In re Brana*, 51 F.3d 1560, 34 USPQ 1436 (Fed. Cir. 1995); *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980); *In re Malachowski*, 530 F.2d 1402, 189 USPQ 432 (CCPA 1976); *In re Gazave*, 379 F.2d 973, 154 USPQ 92 (CCPA 1967); *In re Hartop*, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); *In re Krimmel*, 292 F.2d 948, 130 USPQ 215 (CCPA 1961).

According to the PTO's own guidelines, for a pharmaceutical invention to have utility, it need not be a safe or fully effective drug for humans and *in vitro* data is clearly sufficient to demonstrate utility. Further, as noted above, MPEP 2107.03 explicitly states that if an applicant has initiated human clinical trials then the PTO "should presume that the subject matter of that trial [here proliferation of fibroblast cells and epithelial cells to treat wounds in the lining of the gastrointestinal tract] is reasonably predictive of having the asserted therapeutic utility" (emphasis in original). When, as here, such an FDA reviewed use appears in the specification, then "[Patent] Office personnel must be extremely hesitant to challenge utility." In such circumstances, "Office personnel must be able to carry their burden that there is no sound rationale for the asserted utility even though experts [i.e., the FDA] designated by Congress to decide the issue have come to an opposite conclusion." (emphasis added) MPEP 2107.03 (V). The PTO has not carried its burden.

The Examiner acknowledges that Appellants' specification details an identification of a pharmacologic utility, details the results of *in vitro* experiments supporting the asserted utility, and asserts a real world therapeutic utility (proliferation of fibroblast cells and epithelial cells to treat gastrointestinal wounds). This has been confirmed by evidence of record detailing *in vivo* results (including evidence of entry into human clinical trials) that are reasonably correlated (in fact exactly what Appellant asserted) to the *in vitro* results in the specification.6/ That is all that is required to satisfy the utility requirement.

Lack of Enablement Rejection is Improper

The pending claims were also rejected under 35 U.S.C. § 112 ¶ 1 for lack of enablement. The Examiner alleges that since the claimed invention lacks utility, it follows that one skilled in the art would not know how to use the claimed invention.

In order for the Examiner's position to be upheld on the utility-based § 112, ¶ 1, non-enablement rejection, the specific factual showing must represent one of those rare instances meeting the stringent criterion of being "totally incapable of achieving a useful result" Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555 (Fed. Cir. 1992), as

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6/ See, e.g., Ex. 9, 10, and 11, p. 5, lines 15-21, p. 76, lines 29-30, and p. 77, lines 26-29.